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Carestream Health Inc, 150 Verona Street Rochester, NY 14608			EXAMINER HYUN, PAUL SANG HWA	
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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/625,424
Filing Date: July 23, 2003
Appellant(s): QIAO ET AL.

Susan L. Parulski
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on 12/03/07 appealing from the Office action mailed 04/06/07.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,429,027 B1	Chee et al.	8-2002
2004/0069857 A1	Leblans et al.	4-2004
4663277	Wang	5-1987
4,092,408	Litt	5-1978

(9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims **1-5, 7-12 and 14-17** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al. (US 6,429,027 B1) in view of Leblans et al. (US 2004/0069857 A1).

Chee et al. disclose a two-dimensional array of microspheres randomly immobilized in wells of a substrate (see Figs. 1A, 1B and line 2, col. 5), wherein the concentration of the microspheres can range from a single microsphere to 2 billion microspheres per cm² (see lines 1-33, col. 6). The size of the microspheres can range between 0.2 to 200 microns (see lines 33-40, col. 9). The microspheres bear biological probes in the form of a bioactive agent (i.e. nucleic acids [see claim 12]) that binds an analyte of interest (see claim 1). The microspheres can comprise a dye in the form of chromophores that can be developed to produce a unique optical signature that allows

one to visually identify the microspheres and the bioactive agent bound to the microspheres (see claim 5 and line 25, col. 21). The microspheres disclosed by Chee et al. differ from the claimed invention in that the reference does not disclose that the dye is a colorless dye that can be developed to a colored state.

Leblans et al. disclose photochromic dyes for identifying microspheres (see [0056]). The disclosed photochromic dyes are colorless and undergo an irreversible change in light absorption in the presence of specific wavelengths of electromagnetic radiation. The reference discloses that the photochromic dyes are advantageous because the dye is initially colorless and once it changes color, the color change is irreversible. It would have been obvious to one of ordinary skill in the art to use the photochromic dyes disclosed by Leblans et al. to identify the microspheres disclosed by Chee et al. since the photochromic dyes disclosed by Leblans et al. undergo permanent color change.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Leblans et al. as applied to claims 1-5, 7-12, 14-17, and further in view of Wang (US 4,663,277).

Neither Chee et al. nor Leblans et al. disclose the immobilization of the microspheres by a gelation process.

Wang discloses an immunoassay for a virus accomplished by utilizing microspheres coated with antiviral antibodies. The reference discloses that the method of the immunoassay involves immobilizing the microspheres by placing the

microspheres in a gel (see lines 46-50 col. 9). In light of the disclosure of Wang, it would have been obvious to one of ordinary skill in the art to further immobilize the modified Chee et al. microspheres by means of a gel so that the microspheres are better secured within the wells of the substrate.

Claims **1, 3, 5 and 6** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Litt (US 4,092,408).

Chee et al. disclose a two-dimensional array of microspheres randomly immobilized in wells of a substrate (see Figs. 1A, 1B and line 2, col. 5), wherein the concentration of the microspheres can range from a single microsphere to 2 billion microspheres per cm^2 (see lines 1-33, col. 6). The size of the microspheres can range between 0.2 to 200 microns (see lines 33-40, col. 9). The microspheres bear biological probes in the form of a bioactive agent (i.e. nucleic acids [see claim 12]) that binds an analyte of interest (see claim 1). The microspheres can comprise a dye in the form of chromophores that can be developed to produce a unique optical signature that allows one to visually identify the microspheres and the bioactive agent bound to the microspheres (see claim 5 and line 25, col. 21). The microspheres disclosed by Chee et al. differ from the claimed invention in that the reference does not disclose that the dye is a colorless dye that can be developed to a colored state.

Litt discloses an enzyme label that interacts with colorless o-nitrophenol dyed sugar to produce a measurable color intensity (see lines 45-55, col. 7). The enzyme cleaves the sugar from the dye and releases the dye. The intensity of the color is

proportional to the enzyme activity. It would have been obvious to one of ordinary skill in the art to provide the microspheres disclosed by Chee et al. with the dye label disclosed by Litt since the label disclosed by Litt allows the quantification of enzyme activity directly from the intensity of the color produced by the enzyme reaction.

(10) Response to Argument

Rejection of claims 1-5, 7-12 and 14-17 under 35 U.S.C. § 103(a) over Chee et al. in view of Leblans et al.:

Appellants' arguments with respect to the rejection have been fully considered, but they are not persuasive.

1) Appellants argue that the references fail to disclose a colorless and non-fluorescent molecule. This argument is not persuasive. With respect to the colorless limitation, Leblans et al. disclose that the photochromic dye that is used to identify a microsphere is a colorless dye that undergoes irreversible color change once it is developed (see line 23 of [0056]). With respect to the non-fluorescent limitation, Leblans et al. also disclose that the same photochromic dye is non-fluorescent as evidenced by lines 53-61 of [0056], which distinguish the photochromic dye from fluorescent dyes. Paragraphs [0149]-[0160] of Leblans et al. further distinguish photochromic dyes from fluorescent dyes. The passages of Leblans et al. cited by Appellants in the brief refer to fluorescent dyes, not the photochromic dyes relied upon for rejecting the claims.

2) Appellants also argue that the instant invention has surprising results. This argument is moot since the argument is based on the premise that neither Chee et al.

nor Leblans et al. disclose a colorless, non-fluorescent dye. However, as addressed above, Leblans et al. do disclose a dye that is colorless and non-fluorescent.

Rejection of claim 13 under 35 U.S.C. § 103(a) over Chee et al. in view of Leblans et al. and further in view of Wang:

Appellants' arguments with respect to the rejection have been fully considered, but they are not persuasive.

1) Appellants argue that the references fail to disclose a colorless and non-fluorescent molecule. This argument is not persuasive. As addressed above, Leblans et al. disclose a dye that is both colorless and non-fluorescent. For the sake of brevity, the response to the argument will not be repeated.

2) Appellants also argue that the combination of the references fail to provide a likelihood of success of solving the problem solved by the present invention. This argument is not persuasive. The fact that Appellants have recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In this case, Leblans et al. disclose the advantage of using a photochromic dye over a fluorescent dye for identifying microspheres (see lines 53-61 of [0056]). One advantage disclosed by the passage is that photochroming is potentially faster and easier to control than the bleaching of fluorescent dye. The advantages disclosed in the passage are sufficient motivation to modify the microspheres disclosed by Chee et al.

Rejection of claims 1, 3, 5 and 6 under 35 U.S.C. § 103(a) over Chee et al. in view of Litt:

Appellants' arguments with respect to the rejection have been fully considered, but they are not persuasive.

1) Appellants argue that the references fail to disclose a colorless and non-fluorescent molecule. This argument is not persuasive. With respect to the colorless limitation, Litt discloses that the o-nitrophenol dyed sugar that is used to identify a particle is colorless (see lines 48-55, col. 7). With respect to the non-fluorescent limitation, there is no disclosure in Litt that suggests that the enzyme label or the o-nitrophenol dyed sugar is fluorescent. The passages cited by Appellants in the brief characterize fluorescent dyes, not the enzyme label or the o-nitrophenol dyed sugar relied upon for the rejection.

2) Appellants also argue that Chee et al. and Litt are non-analogous art and that there is no likelihood of success of combining the teachings of the two references. Specifically, Appellants argue that Litt does not disclose that the dyes are compatible with a microarray comprising microspheres because the dye disclosed by Litt releases the dye onto the entire assay, which would prevent identification of individual microspheres. This argument is not persuasive for two reasons. First, according to Chee et al., the array is conducted in wells of a microplate wherein each well can comprise a single microsphere (see column 6). In such an embodiment, identifying individual microsphere would not be hindered by the use of the dye disclosed by Litt. Second, It should be noted that the claims do not recite that the limitation "identify"

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recited in claim 1 refers to distinguishing individual microspheres from other microspheres. Rather, the limitation can be construed to mean "identifying the presence of microspheres bearing a probe of interest", which the dye disclosed by Litt is capable of accomplishing.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,


/Paul S Hyun/


Examiner, Art Unit 1797

Conferees:

/Romulo H. Delmendo/

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